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Serial No.: 09/430,775
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Page 3

Amendments to the Specification:

On page 1, line 6, ~~Background of the Invention:~~

--This application is a continuation of U.S. Serial No. 08/495,695, filed January 13, 1997, ~~now allowed,~~ now U.S. Patent No. 5,976,814, issued November 2, 1999, which was a §371 national stage application of PCT International Application No. PCT/US94/14436, filed December 28, 1994, claiming priority of and a continuation-in-part of U.S. Serial No. 08/176,412, filed December 28, 1993, now U.S. Patent No. 5,516,653, issued May 14, 1996.

Background of the Invention --

On page 11, line 2:

--Brief Description of the Figures Drawings--

On page 11, line 4:

--Figure 1 Figures 1A-1E--

On page 11, lines 5-16:

--Nucleotide sequence and Deduced Amino Acid Sequence of a Novel Human hp25a Neuropeptide Receptor ~~(Sequence I.D. Nos. 1 and 2)~~ (SEQ ID NOS: 1 and 2). Nucleotides are presented in the 5' and 3' orientation and the coding region is numbered starting from the initiating methionine and ending in the termination codon. Deduced amino acid sequence by translation of a long open reading frame is shown, along with the 5' and 3' untranslated regions. Numbers in the left and right margins represent nucleotide (top line) and amino acid (bottom line)

numberings, starting with the first position as the adenosine (A) and the initiating methionine (M), respectively.--

On page 11, line 18:

--~~Figure 2~~ Figures 2A-2C--

On page 11, line 36 through page 12, line 8:

--~~Figure 3.~~ Figures 3A-3D Nucleotide sequence and deduced amino acid sequence of the rat Y4 receptor encoded by rs16b (SEQ ID NOS: 27 and 28). Nucleotides are presented in the 5' to 3' orientation and the coding region is numbered starting from the putative initiating methionine and ending in the termination codon. Deduced amino acid sequence by translation of a long open reading frame is shown, along with 5' and 3' untranslated regions. The amino acid sequence is represented using single-letter abbreviations.--

On page 17, line 29 through page 18, line 15:

--This invention provides vectors comprising isolated nucleic acid molecules such as DNA, RNA, or cDNA encoding a Y4 receptor. In one embodiment the Y4 receptor is a human Y4 receptor. In another embodiment the Y4 receptor is a rat Y4 receptor. Examples of vectors are viruses such as bacteriophages (such as phage lambda), animal viruses (such as Herpes virus, Murine Leukemia virus, and Baculovirus), cosmids, plasmids (such as pUC18, available from Pharmacia, Piscataway, NJ), and other recombination vectors. Nucleic acid molecules are inserted into vector genomes by methods well known in the art. For example, insert and vector DNA can both be exposed to a restriction enzyme to create complementary ends on both molecules which base pair with each

other and are then ligated together with a ligase. Alternatively, linkers can be ligated to the insert DNA which correspond to a restriction site in the vector DNA, which is then digested with the restriction enzyme which cuts at that site. Other means are also available. Specific examples of such plasmids are plasmids comprising cDNA having a coding sequence substantially the same as the coding sequence shown in Figure 1 and designated clone hp25a ~~(Seq. I.D. No. 1)~~ (SEQ ID NO: 1) or the coding sequence shown in Figure 3 and designated clone rs16b ~~(Sequence I.D. No. 27)~~ (SEQ ID NO: 27).--

On page 20, lines 14-20:

--The deposit discussed supra, and the other deposits discussed herein, were made pursuant to, and in satisfaction of, the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure with the American Type Culture Collection (ATCC), ~~12301 Parklawn Drive, Rockville, Maryland 20852~~ 10801 University Boulevard, Manassas, VA 20110-2209.--

On page 33, line 24 through page 34, line 27:

--This invention provides an antibody directed to a Y4 receptor, for example a monoclonal antibody directed to an epitope of a Y4 receptor present on the surface of a cell and having an amino acid sequence substantially the same as an amino acid sequence for a cell surface epitope of the human Y4 receptor included in the amino acid sequence shown in Figure 1 ~~(Seq. I.D. No. 2)~~ (SEQ ID NO: 2) or the rat Y4 receptor included in the amino acid sequence shown in Figure 3 ~~(Seq. I.D. No. 28)~~ (SEQ ID NO: 28). Amino acid sequences may

be analyzed by methods well known in the art to determine whether they produce hydrophobic or hydrophilic regions in the proteins which they build. In the case of cell membrane proteins, hydrophobic regions are well known to form the part of the protein that is inserted into the lipid bilayer which forms the cell membrane, while hydrophilic regions are located on the cell surface, in an aqueous environment. Therefore antibodies to the hydrophilic amino acid sequences shown in Figures 1 and 3 will probably bind to a surface epitope of a human or rat Y4 receptor, respectively, as described. Antibodies directed to Y4 receptors may be serum-derived or monoclonal and are prepared using methods well known in the art. For example, monoclonal antibodies are prepared using hybridoma technology by fusing antibody producing B cells from immunized animals with myeloma cells and selecting the resulting hybridoma cell line producing the desired antibody. Cells such as COS-7 cells or LM(tk-) cells comprising DNA encoding the human Y4 receptor and thereby expressing the human Y4 receptor may be used as immunogens to raise such an antibody. Alternatively, synthetic peptides may be prepared using commercially available machines and the amino acid sequences shown in Figures 1 and 3 (~~Seq. I.D. Nos. 2 and 28~~) (SEQ ID NOS: 2 and 28). As a still further alternative, DNA, such as a cDNA or a fragment thereof, may be cloned and expressed and the resulting polypeptide recovered and used as an immunogen. These antibodies are useful to detect the presence of human Y4 receptors encoded by the isolated DNA, or to inhibit the function of the receptors in living animals, in humans, or in biological tissues or fluids isolated from animals or humans.--

On page 44, line 4 through page 45, line 16:

--Cloning and Sequencing of a human (Y4) Neuropeptide Receptor. A human placenta genomic library in λ dash II (1.5 x 10⁶ total recombinants; Stratagene, LaJolla, CA) was screened using overlapping transmembrane (TM) oligonucleotide probes (TM 1, 2, 3, 5 and 7) derived from the rat Y1 neuropeptide receptor gene (Eva, C. et al., 1990; GenBank accession No. Z11504). Overlapping oligomers (TM1: nts. 198-251, (+)strand/5'-TTGCTTATGGGGCTGTGATTATTCTTGGGGTCTCTGGAAACCTGG-3' ~~(Sequence I.D. No. 3)~~ (SEQ ID NO: 3) and (-)strand/5'-TAGGATGATTATGATCAATGCCAGGTTTCCAGAGACCCCAAGAAT-3' ~~(Sequence I.D. No. 4)~~ (SEQ ID NO: 4); TM2: nts. 269-328, (+)strand/5'-AAAGAGATGAGGAATGTCACCAACATTCTGATCGTGAACCTCTCC-3' ~~(Sequence I.D. No. 5)~~ (SEQ ID NO: 5) and (-)strand/5'-CAGCAAGTCTGAGAAGGAGAGGTTACGATCAGAATGTTGGTGAC-3' ~~(Sequence I.D. No. 6)~~ (SEQ ID NO: 6); TM3: nts. 401-478, (+)strand/5'-TGCAAACCTGAATCCTTTTGTGCAATGCGTCTCCATTACAGTATCCATTTTCTCT-3' ~~(Sequence I.D. No. 7)~~ (SEQ ID NO: 7) and (-) strand/5'-ACGTTCCACAGC
GATGAGAACCAGAGAGAAAATGGATACTGTAATGGAGACGCA-3' ~~(Sequence I.D. No. 8)~~ (SEQ ID NO: 8); TM5: nts. 716-778, (+)strand/5'-CTGCAGTATTTTGGCCCACTCTGTTTCATATTCATATGCTAC-3' ~~(Sequence I.D. No. 9)~~ (SEQ ID NO: 9) and (-)strand/5'-CAAGCGAATGTATATCTTGAAGTAGCATATGAATATGAAACA-3' ~~(Sequence I.D. No. 10)~~ (SEQ ID NO: 10); TM7: nts. 971-1045, (+)strand/5'-CTGCTCTGCCACCTCACGGCCATGATCTCCACCTGCGTCAACC
CCATC-3' ~~(Sequence I.D. No. 11)~~ (SEQ ID NO: 11) and (-)strand/5'-GAAATTTTGTTCAGGAATCCATAAAAGATGGGGTTGA
CGCAGGTGGA-3' ~~(Sequence I.D. No. 12)~~ (SEQ ID NO: 12); GenBank accession No. Z11504) were labeled with [³²P]dATP and [³²P]dCTP

by synthesis with the large fragment of DNA polymerase. Hybridization was performed at low stringency conditions: 40EC. in a solution containing 25.0% formamide, 5x SSC (1X SSC is 0.15M sodium chloride, 0.015M sodium citrate), 1x Denhardt's solution (0.02% polyvinylpyrrolidone, 0.02% Ficoll, 0.02% bovine serum albumin), and 25 µg/µl sonicated salmon sperm DNA. The filters were washed at 40EC. in 0.1x SSC containing 0.1% sodium dodecyl sulfate and exposed at -70EC. to Kodak XAR film in the presence of an intensifying screen. Lambda phage clones hybridizing with the probes were plaque purified and DNA was prepared for Southern blot analysis (Southern, 1975; Sambrook et al., 1989). A Genomic clone hybridizing with all five of the rat Y1 TM probes, designated hp25a, was isolated using this method. For subcloning and further Southern blot analysis, **the hp25a** DNA was cloned into pUC18 (Pharmacia, Piscataway, NJ). Nucleotide sequence analysis was accomplished by the Sanger dideoxy nucleotide chain termination method (Sanger et al., 1977) on denatured double-stranded plasmid templates, using Sequenase (US Biochemical Corp., Cleveland, OH).--

Attached hereto as **Exhibit A** are nineteen (19) sheets of new, corrected drawings for Figures 1A through 9B which replace original Figures 1-1 through 9B.